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Chapter

Pneumococcal Disease

DISEASE CAUSED BY *STREPTOCOCCUS PNEUMONIAE,* RESULTS IN wide-spread illness and death throughout the United States each year. The bacterium, also called pneumococcus, was first identified by Pasteur in 1881 from the saliva of a patient with rabies. The association between the pneumococcus bacterium and lobar pneumonia was first described by Friedlander and Talamon in 1883, but pneumococcal pneumonia was confused with other types of pneumonia until the discovery of the Gram stain in 1884. From 1915 to 1945, the chemical structure and antigenicity of the pneumococcal capsular polysaccharide, its association with virulence, and the role of bacterial polysaccharides in human disease were explained. More than 80 serotypes of pneumococci had been described by 1940.

Pneumococcal Disease

- ***S. pneumoniae*** **first isolated by Pasteur in 1881**
- **Confused with other causes of pneumonia until discovery of Gram stain in 1884**
- **Structure and role of capsule determined by 1945**
- **First vaccine licensed in U.S. in 1977**

Efforts to develop effective pneumococcal vaccines began as early as 1911. However, with the advent of penicillin in the 1940s, interest in the vaccine declined, until it was observed that many patients still died despite antibiotic treatment. By the late 1960s, efforts were again being made to develop a polyvalent pneumococcal vaccine. The first pneumococcal vaccine was licensed in the United States in 1977. The first conjugate pneumococcal vaccine was licensed in 2000.

Streptococcus pneumoniae

Streptococcus pneumoniae are lancet-shaped, gram-positive, facultative anaerobic organisms. They are typically observed in pairs (diplococci) but may also occur singularly or in short chains. Some pneumococci are encapsulated, their surfaces composed of complex polysaccharides. Encapsulated organisms are pathogenic for humans and experimental animals, whereas organisms without capsular polysaccharides are not. Capsular polysaccharides are the primary basis for the pathogenicity of the organism. They are antigenic and form the basis for classifying pneumococci by serotypes. Ninety serotypes

Streptococcus pneumoniae

- **Gram-positive bacteria**
- **90 known serotypes**
- **Polysaccharide capsule important virulence factor**
- **Type-specific antibody is protective**

have been identified, based on their reaction with type-specific antisera. Type-specific antibody to capsular polysaccharide is protective. These antibodies and complement interact to opsonize pneumococci, which facilitates phagocytosis and clearance of the organism. Antibodies to some pneumococcal capsular polysaccharides may cross-react with related types as well as with other bacteria, providing protection to additional serotypes.

Pneumococcal Disease Clinical Syndromes

- **Pneumonia**
- **Bacteremia**
- **Meningitis**

Most *S. pneumoniae* serotypes have been shown to cause serious disease, but only a few serotypes produce the majority of pneumococcal infections. The 10 most common serotypes are estimated to account for about 62% of invasive disease worldwide. The ranking and serotype prevalence differs by age group and geographic area. In the United States the seven most common serotypes isolated from the blood or CSF of children <6 years of age account for 80% of infections. These 7 serotypes account for only about 50% of isolates from older children and adults.

Pneumococci are common inhabitants of the respiratory tract, and may be isolated from the nasopharynx of 5% to 70% of normal adults. Rates of asymptomatic carriage vary with age, environment, and the presence of upper respiratory infections. Only 5%-10% of adults without children are carriers. In schools and orphanages, 27% to 58% of students and residents may be carriers. On military installations, as many as 50% to 60% of service personnel may be carriers. The duration of carriage varies and is generally longer in children than adults. In addition, the relationship of carriage to the development of natural immunity is poorly understood.

Pneumococcal Pneumonia Clinical Features

- **Abrupt onset**
- **Fever**
- **Shaking chills**
- **Productive cough**
- **Pleuritic chest pain**
- **Dyspnea, tachypnea, hypoxia**

Clinical Features

The major clinical syndromes of invasive pneumococcal disease include **pneumonia**, **bacteremia**, and **meningitis**. The immunologic mechanism that allows disease to occur in a carrier is not clearly understood. However, disease most often occurs when a predisposing condition exists, particularly pulmonary disease.

Pneumococcal Pneumonia

- **Estimated 150,000 - 570,000 cases per year**
- **Up to 36% of adult community-acquired pneumonia and 50% of hospital-acquired pneumonia**
- **Common bacterial complication of influenza and measles**
- **Case-fatality rate 5%-7%, higher in elderly**

Pneumococcal pneumonia is the most common clinical presentation of invasive pneumococcal disease among adults. The **incubation period** of pneumococcal pneumonia is short, about 1 to 3 days. Symptoms generally include an abrupt onset of fever and shaking chills or rigors. Typically there is a single rigor, and repeated shaking chills are uncommon. Other common symptoms include pleuritic chest pain, cough productive of mucopurulent, rusty sputum, dyspnea (shortness of breath), tachypnea (rapid breathing), hypoxia

(poor oxygenation), tachycardia (rapid heart rate), malaise, and weakness. Nausea, vomiting, and headaches occur less frequently.

An estimated 150,000 - 570,000 cases of pneumococcal pneumonia occur annually in the United States. Pneumococci account for up to 36% of adult community-acquired pneumonia and 50% of hospital-acquired pneumonia. It is a common bacterial complication of influenza and measles. The case-fatality rate is 5%-7%, and may be much higher in elderly persons. Complications of pneumococcal pneumonia include empyema (i.e., infection of the pleural space), pericarditis, or inflammation of the sac surrounding the heart, and endobronchial obstruction, with atelectasis and lung abscess formation.

An estimated 16,000 to 55,000 cases of **pneumococcal bacteremia** occur each year. Bacteremia occurs in about 25%-30% of patients with pneumococcal pneumonia. The overall mortality rate for bacteremia is about 20%, but may be as high as 60% in elderly patients. Patients with asplenia who develop bacteremia may experience a fulminant clinical course.

Pneumococcal Bacteremia

- **Estimated 16,000 - 55,000 cases per year in the United States**
- **Rates higher among elderly and very young infants**
- **Case fatality rate ~20%; up to 60% among the elderly**

Pneumococci cause 13%-19% of all cases of **bacterial meningitis** in the United States. An estimated 3,000 to 6,000 cases of pneumococcal meningitis occur each year. One-quarter of patients with pneumococcal meningitis also have pneumonia. The clinical symptoms, spinal fluid profile and neurologic complications are similar to other forms of purulent bacterial meningitis. Symptoms may include headache, lethargy, vomiting, irritability, fever, nuchal rigidity, cranial nerve signs, seizures and coma. The mortality rate of pneumococcal meningitis is about 30%, but may be as high as 80% in elderly persons. Neurologic sequelae are common among survivors.

Pneumococcal Meningitis

- **Estimated 3,000 - 6,000 cases per year in the United States**
- **Case-fatality rate ~30%, up to 80% in the elderly**
- **Neurologic sequelae common among survivors**

Pneumococcal disease in children

Bacteremia without a known site of infection is the most common invasive clinical presentation among children <2 years of age, accounting for approximately 70% of invasive disease in this age group. Bacteremic pneumonia accounts for 12%-16% of invasive pneumococcal disease among children <2 years of age. With the decline of invasive Hib disease, S. pneumoniae has become the leading cause of bacterial meningitis among children <5 years of age in the United States. Children <1 year have the highest rates of pneumococcal meningitis, approximately 10 cases per 100,000 population.

Pneumococcal Disease in Children

- **Bacteremia without known site of infection most common invasive clinical presentation**
- **S. pneumoniae leading cause of bacterial meningitis among children <5 years of age**
- **Common cause of acute otitis media**

Pneumococci are a common cause of acute otitis media, and are detected in 28%-55% of middle ear aspirates. By age 12 months, 62% of children have had at least one episode of acute otitis media. Middle ear infections are the most frequent reasons for pediatric office visits in the United States, resulting in over 20 million visits annually. Complications of pneumococcal otitis media may include mastoiditis and meningitis.

Laboratory Diagnosis

A definitive diagnosis of infection with *Streptococcus pneumoniae* generally relies on **isolation of the organism** from blood or other normally sterile body sites. Tests are also available to detect capsular polysaccharide antigen in body fluids.

The appearance of lancet-shaped diplococci on **Gram stain** is suggestive of pneumococcal infection, but interpretation of stained sputum specimens may be difficult because of the presence of normal nasopharyngeal bacteria. The suggested criteria for obtaining a diagnosis of pneumococcal pneumonia using Gram stained sputnum includes >25 white blood cells and <10 epithelial cells per 100-power field, and a predominance of gram-positive diplococci.

The **quellung reaction** (capsular swelling; capsular precipitation reaction) is a test that provides rapid identification of pneumococci in clinical specimens including spinal fluid, sputum, and exudates. The procedure involves mixing loopfuls of bacteria in suspension, pneumococcal antiserum, and methylene blue on the surface of a glass slide and examination under oil immersion. If the reaction is positive, the organism will be surrounded by a large capsule.

Counterimmunoelectrophoresis (CIE) is a rapid and specific diagnostic method to detect pneumococcal capsular polysaccharide antigen in various specimens including blood, spinal fluid, urine, pleural fluid, and peritoneal fluid. Sensitivity is highest in spinal fluid. The latex or co-agglutination test is similar to the CIE, but has the advantages of being easier to perform and more sensitive for detecting antigen in spinal fluid. None of the rapid tests are useful for diagnosing pneumonia using sputum, because of poor specificity.

Medical Management

Penicillin is the drug of choice for treatment of pneumococcal disease. However, patients who are allergic to penicillin may be given cephalosporins (depending on the severity of the penicillin allergy) or erythromycin for pneumonia, and chloramphenicol for meningitis. The route, dosage, schedule, and duration of therapy depend on the severity of the illness. Resistance to penicillin and other antibiotics is rising. In some areas of the U.S. up to 35% of invasive pneumococcal isolates are not susceptible to penicillin.

Epidemiology

Occurrence

Pneumococcal disease occurs throughout the world.

Pneumococcal Disease Epidemiology

• Reservoir	Human carriers
• Transmission	Respiratory "Autoinoculation"
• Communicability	Unknown Probably as long as organism in respiratory secretions

Reservoir

Streptococcus pneumoniae is a human pathogen. The reservoir for pneumococci is presumably the nasopharynx of asymptomatic human carriers. There is no animal or insect vector.

Transmission

Transmission of *Streptococcus pneumoniae* occurs as the result of direct person-to-person contact via droplets, and by "autoinoculation" in persons carrying the bacteria in their upper respiratory tract. The pneumococcal serotypes most often responsible for causing infection are those most frequently found in carriers. The spread of the organism within a family or household is influenced by such factors as crowding, season, and the presence of upper respiratory infections or pneumococcal disease such as pneumonia or otitis media. The spread of pneumococcal disease is usually associated with increased carriage rates. However, high carriage rates do not appear to increase the risk of disease transmission in households.

Temporal pattern

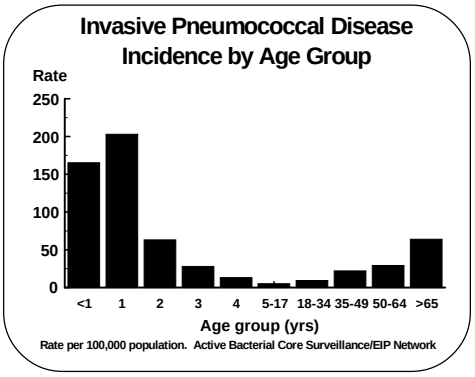
Pneumococcal infections are more common during the winter and in early spring when respiratory diseases are more prevalent.

Communicability

The period of communicability for pneumococcal disease is unknown, but presumably transmission can occur as long as the organism appears in respiratory secretions.

Secular Trends in the United States

Estimates of the incidence of pneumococcal disease have been made from a variety of population-based studies. Over 50,000 cases of invasive pneumococcal disease (meningitis and bacteremia) are believed to occur annually in the United States. In addition, there are hundreds of thousands of cases of non-bacteremic pneumonia, and millions of cases of otitis media which are considered non-invasive infections.



The overall incidence of invasive pneumococcal disease (bacteremia, meningitis, or other infection of a normally sterile site) in the United States is estimated to be approximately 21 cases per 100,000 population. However, incidence rates vary greatly by age group. **The highest rates of invasive pneumococcal disease occur in young children, especially those <2 years of age.** Incidence among children <12 months of age in 1998 was estimated at 165 cases per 100,000 population, and among children 12-13 months, 203 cases per 100,000 population. Incidence is lowest in persons 5-17 years of age, and increase to 61 per 100,000 population in persons 65 years of age and older.

Children at Increased Risk of Invasive Pneumococcal Disease

- **Functional or anatomic asplenia, especially sickle cell disease**
- **HIV infection**
- **Alaskan native, American Indian, African American**
- **Day care attendance**

Children with functional or anatomic asplenia, particularly those with sickle cell disease, and children with HIV infection are at very high risk of invasive disease, with rates in some studies more than 50 times higher than children of the same age without these conditions (*i.e.*, incidence rates of 5,000-9,000 per 100,000 population). Children of certain racial and ethnic groups have increased rates, in particularly children of Alaskan Native, certain American Indian groups, and of African American origin. The reason for this increased risk by race and ethnicity is not known with certainty, but was also noted for invasive *Haemophilus influenzae* infection (also an encapsulated bacteria). Attendance at a day care center has also been shown to increase the risk of invasive pneumococcal disease and acute otitis media from 2-3-fold among children <59 months of age.

Mortality from pneumococcal disease is highest among patients with bacteremia or meningitis, in patients with underlying medical conditions, and in very young or older persons. Among some high-risk patients, up to 40% of

those with bacteremic disease die. High death rates from bacteremia occur despite therapy with antibiotics. Fatality rates increase from 30%-40% in those 50 to 69 years of age to 55%-60% in persons 70 or older.

Community-acquired pneumococcal pneumonia is usually a sporadic disease in carriers who have a breakdown in their pulmonary defense mechanisms. Secondary pneumococcal pneumonia is the most common bacterial complication of both influenza and measles. However, epidemics of pneumococcal pneumonia are uncommon. When epidemics occur, they are usually in crowded environments, such as jails and nursing homes. During outbreaks, persons with invasive disease often have underlying illness and may have a high fatality rate.

Pneumococcal Disease Outbreaks

- **Outbreaks uncommon**
- **Generally occur in crowded environments (jails, nursing homes)**
- **Persons with invasive disease often have underlying illness**
- **May have high fatality rate**

Pneumococcal Vaccines

Characteristics

Pneumococcal polysaccharide vaccine

Pneumococcal polysaccharide vaccine is composed of purified preparations of pneumococcal capsular polysaccharide. The first polysaccharide pneumococcal vaccine was licensed in the United States in 1977. It contained purified capsular polysaccharide antigen from 14 different types of pneumococcal bacteria. In 1983, a 23-valent polysaccharide vaccine (PPV23) was licensed and replaced the 14- valent vaccine, which is no longer produced. PPV23 contains polysaccharide antigen from the 23 types of pneumococcal bacteria that cause 88% of bacteremic pneumococcal disease. In addition, cross-reactivity occurs for several capsular types which account for an additional 8% of bacteremic disease.

Pneumococcal Vaccines

- **1977 14-valent polysaccharide vaccine licensed**
- **1983 23-valent polysaccharide vaccine licensed**
- **2000 7-valent polysaccharide conjugate vaccine licensed**

Two polysaccharide vaccines are available in the United States (Pneumovax 23, Merck, and Pnu-Immune 23, Lederle). Both vaccines contain 25 mcg of each antigen per dose and include either phenol or thimerosal as a preservative. Pneumococcal vaccine is given by injection, and may be administered either intramuscularly or subcutaneously.

Pneumococcal conjugate vaccine

The first pneumococcal conjugate vaccine (PCV7) was licensed in the United States in 2000. It includes purified capsular polysaccharide of 7 serotypes of *S. pneumoniae* (4, 9V, 14, 19F, 23F, 18C, and 6B) conjugated to a nontoxic

variant of diphtheria toxin known as CRM197. The serotypes included in PCV7 accounted for 86% of bacteremia, 83% of meningitis, and 65% of acute otitis media among children <6 years of age in the United States during 1978-1994. Additional pneumococcal polysaccharide conjugate vaccines containing nine and 11 serotypes of *S. pneumoniae* are being developed. The vaccine is administered intramuscularly.

Immunogenicity and vaccine efficacy

Pneumococcal polysaccharide vaccine

More than 80% of healthy adults who receive PPV23 develop antibodies against the serotypes contained in the vaccine, usually within 2 to 3 weeks after vaccination. Older adults, and persons with some chronic illnesses or immunodeficiency may not respond as well, if at all. In children under 2 years of age, antibody response to most serotypes is generally poor. Elevated antibody levels persist for at least 5 years in healthy adults, but fall more quickly in persons with certain underlying illnesses.

Pneumococcal Polysaccharide Vaccine

- **Purified pneumococcal polysaccharide (23 serotypes)**
- **Not effective in children <2 years**
- **60%-70% against invasive disease**
- **Less effective in preventing pneumococcal pneumonia**

PPV23 vaccine efficacy studies have resulted in various estimates of clinical effectiveness. Overall, the vaccine is 60%-70% effective in preventing invasive disease. The vaccine appears to be less effective in preventing nonbacteremic pneumococcal pneumonia. The vaccine may be less effective in preventing pneumococcal infection in some groups, particularly those with significant underlying illness. Although the vaccine may not be as effective in some persons, especially those who do not have normal resistance to infections, it is still recommended for such persons because they are at high risk of developing severe disease.

Studies comparing patterns of pneumococcal carriage before and after PPV23 vaccination have not shown clinically significant decreases in carrier rates among vaccinees. In addition, no change in the distribution of vaccine-type and non-vaccine-type organisms have been observed as the result of vaccination.

Pneumococcal conjugate vaccine

After 4 doses of PCV7 vaccine, virtually all healthy infants develop antibody to all 7 serotypes contained in the vaccine. PCV7 has also been shown to be immunogenic in infants and children, including those with sickle cell disease and HIV infection. In a large clinical trial, PCV7

was shown to reduce invasive disease caused by vaccine serotypes by 97%, and reduce invasive disease caused by all serotypes, including serotypes not in the vaccine, by 89%. Efficacy against pneumonia varied depending on the specificity of the diagnosis. The vaccine reduced clinically diagnosed pneumonia by 11%, but reduced pneumonia confirmed with X-ray with consolidation of >2.5 centimeters by 73%. Children who received PCV7 had 7% fewer episodes of acute otitis media and underwent 20% fewer tympanostomy tube placements than unvaccinated children. The duration of protection following PCV7 is currently unknown. The effect of PCV7 on nasopharyngeal carriage of pneumococci is not clear at this time.

Pneumococcal Conjugate Vaccine

- **Pneumococcal polysaccharide conjugated to nontoxic diphtheria toxin (7 serotypes)**
- **Immunogenic in infants and young children**
- **>90% effective against invasive disease**
- **Less effective against pneumonia and acute otitis media**

Vaccination Schedule and Use

Pneumococcal polysaccharide vaccine

Pneumococcal polysaccharide vaccine should be administered routinely to **all adults 65 years of age and older.** The vaccine is also indicated for **adults with normal immune systems who have chronic illnesses,** including cardiovascular disease, pulmonary disease, diabetes, alcoholism, cirrhosis, or cerebrospinal fluid leaks.

Pneumococcal Polysaccharide Vaccine Recommendations

- **Adults ≥ 65 years of age**
- **Adults with normal immune systems who have chronic illness**
- **Immunocompromised adults**
- **Persons with HIV infection**
- **Persons in environments or settings with increased risk**

Immunocompromised adults who are at increased risk of pneumococcal disease or its complications should also be vaccinated. This group includes persons with splenic dysfunction or absence (either from disease or surgical removal), Hodgkin's disease, lymphoma, multiple myeloma, chronic renal failure, nephrotic syndrome (a type of kidney disease), or conditions such as organ transplantation associated with immunosuppression. Adults with asymptomatic or symptomatic HIV infection should be vaccinated.

Children 2 years old and older with long-term illnesses that are associated with a high risk of serious pneumococcal infections or its complications should be vaccinated.

Pneumococcal Polysaccharide Vaccine Recommendations for Children

- **Recommended for children ≥2 years at high risk of invasive disease**
  - **Splenic absence**
  - **Sickle cell disease**
  - **Nephrotic syndrome**
  - **CSF leaks**
  - **Immunosuppression, including HIV infection**

Children at high risk include whose spleens have been surgically removed, as well as those who have sickle cell disease, nephrotic syndrome, or CSF leaks. **Children with immunosuppression,** including those with asymptomatic or symptomatic HIV, should be vaccinated.

Pneumococcal vaccine should be considered for persons living in special environments or social settings with an identified increased risk of pneumococcal disease or its complications, such as certain Native American populations.

If elective splenectomy is being considered, the vaccine should be given at least 2 weeks before the operation. Similarly, there should also be a two-week interval between vaccination and initiation of cancer chemotherapy or other immunosuppressive therapy.

Providers should not withhold vaccination in the absence of an immunization record or complete record. The patient's verbal history may be used to determine vaccination status. **Persons with uncertain or unknown vaccination status should be vaccinated.**

Pneumococcal conjugate vaccine

All children <24 months of age should be routinely vaccinated with PCV7. The primary series consists of three doses routinely given at 2, 4, and 6 months of age. A fourth (booster) dose is recommended at 12-15 months of age. PCV7 should be administered at the same time as other routine childhood immunizations, using a separate syringe and injection site. For children vaccinated at <12 months of age, the minimum interval between doses is 4 weeks. Doses given at >12 months of age should be separated by at least 8 weeks.

Pneumococcal Conjugate Vaccine Recommendations

- **Routine vaccination of children <24 months of age**
- **Routine schedule 2, 4, 6 months, booster dose at 12-15 months**
- **Unvaccinated children ≥7 months require fewer doses**

Unvaccinated children 7 months of age and older do not require a full series of 4 doses. The number of doses a child needs to complete the series depends on the child's current age. Unvaccinated children aged 7-11 months should receive two doses of vaccine, at least 4 weeks apart, followed by a booster dose at age 12-15 months. Unvaccinated children aged 12-23 months should receive two doses of vaccine, at least 8 weeks apart.

Any previously unvaccinated healthy child aged 24-59 months should receive a single dose of vaccine.

Pneumococcal Conjugate Vaccine

- **Consider vaccination of all children 24-59 months of age**
- **Priority given to children 24-59 months at increased risk:**
  - **24-35 months of age**
  - **Alaskan native, American Indian, African-American**
  - **attend group day care**

ACIP recommends that health care providers consider PCV7 for all children aged 24-59 months, with priority given to children aged 24-35 months, children of Alaskan Native, American Indian or African American descent, and children who attend group day care (defined as any setting outside the home where a child regularly spends >4 hours per week with >2 unrelated children under adult supervision). Healthy unvaccinated children 24-59 months of age should receive a single dose of PCV7. Children 24-59 months of age with sickle cell disease, asplenia, HIV infection, chronic illness, or immunocompromising conditions should receive 2 doses of PCV7 separated by at least 8 weeks.

PCV7 is not routinely recommended for persons >60 months of age.

Few data are available the use of PCV7 among children previously vaccinated with PPV23. Children 24-59 months of age who have already received PPV23 and who are at high risk of invasive pneumococcal disease (sickle cell disease, asplenia, HIV infection or other immuno-compromising conditions or chronic diseases) could benefit from the immunologic priming induced by PCV7. ACIP recommends these children receive 2 doses of PCV7 separated by at least 8 weeks. The first dose of PCV7 should be given no sooner than 2 months after PPV23. Similarly, children 24-59 months of age who have already received one or more doses of PCV7 and who are at high risk of invasive pneumococcal disease will benefit from the additional serotypes included in PPV23. Vaccination with PPV23 should be considered for these high risk children. PPV23 should be given no sooner than 2 months after the last dose of PCV7. Routine administration of PPV23 to healthy children 24-59 months of age is not recommended.

Pneumococcal Conjugate Vaccine

- **Children 24-59 months of age at high risk who have already received PPV23 should receive 2 doses of PCV7**
- **Children at high risk who received PCV7 should receive PPV23 at ≥2 years of age**

Revaccination

Pneumococcal polysaccharide vaccine

Following vaccination with PPV23, antibody levels decline after 5-10 years and decrease more rapidly in some groups than others. However, the relationship between antibody titer and protection from invasive disease is not certain (*i.e.*, higher antibody level does not necessarily mean better protection), so the ability to define the need for revaccination based only on serology is limited. In addition, currently available pneumococcal polysaccharide vaccines elicit a T-independent response, and do not produce a sustained increase ("boost") in antibody titers. Available data do not indicate a substantial increase in protection in the majority of revaccinated persons.

Pneumococcal Polysaccharide Vaccine Revaccination

- **Routine revaccination of immunocompetent persons is not recommended**
- **Revaccination recommended for those at highest risk of serious pneumococcal infection**
- **Single revaccination dose ≥5 years after first dose**

Because of the lack of evidence of improved protection with multiple doses of pneumococcal vaccine, **routine revaccination of immunocompetent persons previously vaccinated with 23-valent polysaccharide vaccine is not recommended.**

However, revaccination is recommended for persons 2 years of age and older who are at highest risk for serious pneumococcal infection and for those who are likely to have a rapid decline in pneumococcal antibody levels. **Only one PPV23 revaccination dose is recommended for high-risk persons.** The second dose should be

administered five or more years after the first dose. Revaccination 3 years after the previous dose may be considered for children at highest risk for severe pneumococcal infection who would be aged 10 years or less at the time of revaccination, including children who received PCV7.

Pneumococcal Polysaccharide Vaccine Candidates for Revaccination

- **Persons >2 years of age with:**
  - **Functional or anatomic asplenia**
  - **Immunosuppression**
  - **Transplant**
  - **Chronic renal failure**
  - **Nephrotic syndrome**
- **Persons vaccinated at <65 years of age**

Persons at highest risk include all people >2 years of age with functional or anatomic asplenia (*e.g.*, sickle cell disease or splenectomy), HIV infection, leukemia, lymphoma, Hodgkins disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome, or other conditions associated with immunosuppression (*e.g.*, organ or bone marrow transplantation) and those receiving immunosuppressive chemotherapy, including long-term corticosteroids.

Persons aged 65 years and older should be administered a second dose of pneumococcal vaccine if they received the vaccine more than 5 years previously, and were less than 65 years of age at the time of the first dose.

Pneumococcal conjugate vaccine

Revaccination after an age-appropriate primary series with PCV7 is not currently recommended.

Adverse Reactions Following Vaccination

Pneumococcal polysaccharide vaccine

The most common adverse reactions following either pneumococcal polysaccharide or conjugate vaccine are **local reactions.** For PPV23, from 30% to 50% of vaccinees report pain, swelling, or erythema at the site of injection. These reactions usually persist for less than 48 hours.

Local reations are reported more frequently following a second dose of PPV23 vaccine than following the first dose. Moderate **systemic reactions** (such as fever and myalgias) are uncommon (<1% of vaccinees), and more severe systemic adverse events are rare.

A transient increase in HIV replication has been reported following PPV23 vaccine. No clinical or immunologic deterioration has been reported in these persons.

Pneumococcal conjugate vaccine

Local reactions following PCV7 occur in 10%-20% of recipients. Less than 3% of local reactions are considered to be severe (e.g., tenderness that interferes with limb movement). Local reactions are more common with the fourth dose than with the first 3 doses. In clinical trials of pneumococcal conjugate vaccine, fever >38°C within 48 hours of any dose of the primary series was reported in 15%-24% of children. However, in these studies, whole cell pertussis vaccine was administer simultaneously with each dose, and some or most of the reported febrile episodes may be attributable to the DTP. In one study acellular pertussis vaccine (DTaP) was given at the same visit as the booster dose of PCV7. In this study, 11% of recipients had a temperature <39°C. Surveillance for less common adverse reactions will be conducted as vaccine use becomes more common. No severe adverse events attributable to PCV7 have been reported.

Pneumococcal Vaccines Adverse Reactions

• Local reactions	
– Polysaccharide	30%-50%
– Conjugate	10%-20%
• Fever, myalgias	
– Polysaccharide	<1%
– Conjugate	5%-24%
• Severe adverse reactions	rare

Contraindications and Precautions to Vaccination

For both pneumococcal polysaccharide and conjugate vaccines, a **serious allergic reaction** to a dose of pneumococcal vaccine or a vaccine component is a contraindication to further doses of vaccine. Such allergic reactions are rare. Persons with **moderate or severe acute illness** should not be vaccinated until their condition improves. However, minor illnesses, such as upper respiratory infections, are not a contraindication to vaccination.

Pneumococcal Vaccines Contraindications and Precautions

- **Severe allergic reaction to prior dose of vaccine or vaccine component**
- **Moderate to severe acute illness**

The safety of PPV23 vaccine for pregnant women has not been studied. It should generally not be given to healthy pregnant women. Women who are at high risk of pneumococcal disease and who are candidates for pneumococcal vaccine should be vaccinated before pregnancy.

Vaccine Storage and Handling

Pneumococcal polysaccharide vaccine should be shipped in an insulated container with coolant packs. Although pneumococcal polysaccharide vaccine can tolerate room temperature for a few days, CDC recommends that the vaccine be stored at refrigerator temperature (2°-8°C [35°-46°F])

Pneumococcal conjugate vaccine should be stored at refrigerator temperature. **Pneumococcal vaccines must not be frozen.**

Opened multidose vials may be used until the expiration date printed on the package if not visibly contaminated.

Goals and Coverage Levels

Pneumococcal Vaccine Coverage

- **Healthy People 2000 goal: 60% coverage for high-risk persons**
- **1997 BRFSS: 45% of persons ≥ 65 years of age ever vaccinated**
- **Vaccination levels lower for black (30%) and hispanic (34%) persons**

The target groups for pneumococcal polysaccharide vaccine and influenza vaccine overlap. These vaccines can be given at the same time at different sites without increased side effects. The Healthy People 2000 goal is to achieve 60% coverage for pneumococcal polysaccharide vaccine among persons at highest risk of pneumococcal disease. Data from the 1997 Behavioral Risk Factor Surveillance System (BRFSS, a population-based, random-digit-dialed telephone survey of the non-institutionalized U.S. population 18 years of age and older) indicate that 45% of persons 65 years of age or older had ever received pneumococcal polysaccharide vaccine, an increase of 9% since the 1995 survey. Vaccination levels increased in all but 4 states and were significantly lower among black and hispanic persons than among white persons.

Pneumococcal Polysaccharide Vaccine Missed Opportunities

- **>65% of patients with severe pneumococcal disease had been hospitalized within preceding 3-5 years but had not been immunized**
- **May be administered simultaneously with influenza vaccine**

Opportunities to vaccinate high-risk persons are missed both at the time of hospital discharge and during visits to clinicians' offices. Effective programs for vaccine delivery are needed, including offering the vaccine in hospitals at discharge, clinicians' offices, nursing homes, and other chronic care facilities.

Pneumococcal Disease Summary

- **Most common cause of death from vaccine-preventable disease**
- **Highest incidence in young children and older adults**
- **Low coverage among adults**
- **New conjugate vaccine for infants and children**

More than two-thirds of the persons who have been hospitalized with serious pneumococcal disease had been admitted to a hospital in the preceding 3 to 5 years. In addition, persons who frequently visit physicians and who have chronic conditions are more likely to be at high risk of pneumococcal infection than those who require infrequent visits. Screening and subsequent immunization of hospitalized persons found to be at high risk could have a significant impact in reducing complications and death associated with pneumococcal disease.

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